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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/833,017	04/10/2001	Dennis Cvitkovitch	1889-00401	8365

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EXAMINER	
BASKAR, PADMAVATHI	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 03/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/833,017	CVITKOVITCH ET AL.	
	Examiner	Art Unit	
	Padmavathi v Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-28,38-56 and 58-68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *23, 24, 26 and 42* is/are allowed.

6)☒ Claim(s) *25,27,28,38-41,43-56 and 58-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *11/24/03*.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION (RCE)

Applicants' Amendment

1. Applicant's amendment filed on 10/16/03 and 12/24/03 in response to the Final Office Action mailed on 7/17/03 is acknowledged.

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/16/03 has been entered.

Status of Claims

3. Claims 1-22, 29-37 and 57 are canceled.

Claims 23-28, 38-43, 45 –48, 50-52, and 54-56 have been amended.

New claims 58-68 have been added.

Claim 42 is withdrawn from consideration as the claim is drawn to SEQ.ID.NO: 16, which was not elected or examined or searched in the previous Office Actions. However, claim 42 now has been amended to recite the elected SEQ.ID.NO: 4 and therefore, is added to the elected invention. Claims 23-28, 38-56 and 58-68 are under prosecution.

Prior Citation of References

4. The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-Form892 or form PTO-Form1449 have been previously cited and made of record.

Prior Citation of Title 35 Sections

5. The text of those sections of Title 35 U.S. Code not included in this action can be

found in a prior Office Action.

Objection withdrawn

6. In view of arguments of record, the new matter objection into the disclosure under 35 U.S.C. 132 is withdrawn.

Rejection Maintained

7. The New Matter Rejection to the claims 38-41 and 43-44 is maintained for the reasons of record as set forth in the Final Office action

Claims 38-41 and 43-44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The added material which is not supported by the original disclosure is as follows: Recitation of 1-15 amino acids from the N-and/or COOH terminal of SEQ.ID.NO: 2 or 4 have been removed and 1 point mutation per each 10amino acids of SEQ.ID.NO: 2 or 4, or portion thereof are not disclosed either in the specification or in the originally presented claims.

This rejection is maintained for essentially the same reasons as the rejection of claims under this statutory provision, as set forth above in the last Office action as stated above. Applicants' arguments filed on 10/16/03 have been fully considered but they are not deemed to be persuasive.

Applicant asserts that paragraph 21, 53 and 54 of the present specification teaches the recited modifications to SEQ.ID.NO: 2 or 4 and 1-25 amino acids have been removed in SEQ.ID.NO: 2 to obtain SEQ.ID.NO: 4. Therefore, applicant requests the examiner to reconsider and withdraw the rejection.

The examiner disagrees with the applicant because paragraph 21, 53 and 54 do not disclose that 1-15 amino acids from the N-and/or COOH terminal of SEQ.ID.NO: 2 or 4

have been removed and 1 point mutation per each 10amino acids of SEQ.ID.NO: 2 or 4, or portion thereof. Further, the modified fragments have not been shown to contain having activity for inhibiting the competence signal activity of the polypeptide of SEQ ID NO: 2 or 4, said polypeptide isolated from S.mutans. (Please note the below written description and enablement rejections).

Claim Rejections - 35 USC 112, first paragraph

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 25, 27-28, 38-41, 43-44, 45, 46, 47-56, 58-68 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims are drawn to an isolated polypeptide having at least 40%, 45%, 60% or 90% amino acid sequence identity to SEQ ID NO: 2 or 4 and having competence signal peptide activity or having activity for inhibiting the competence signal activity of the polypeptide of SEQ ID NO: 2 or 4, said polypeptide isolated from S.mutans.

Claims are also drawn to fragments of SEQ.ID.NO: 2 or 4 having an amino acid sequence ranging from 1-15 amino acids removed from the N- and/or COOH terminal of SEQ ID NO: 2 or 4 (The examiner is considering all these as variants of SEQ.ID.NO: 2 or 4

and will be referred to fragments/variants in this action).

The specification discloses a recombinant polypeptide SEQ ID NO: 2 (46 amino acids) having competence signal peptide activity to S.mutans histidine kinase. The proteolytic cleavage site was predicted to arise immediately after a double lysine consensus sequence in SEQ.ID.NO: 2, which is commonly observed at the end of leader peptide produced in all CSP of gram-positive bacteria. The leader peptide in the present invention is SEQ.ID.NO: 2. The amino acid sequence of the CSP, SEQ.ID.NO: 4 was deduced to be a 21 peptide at the carboxyl terminal of the CSP polypeptide SEQ ID NO: 2. However, the role of these fragments/variants in Gram-positive bacteria has not yet been identified. Further, the specification does not disclose :

(1) an isolated polypeptide having at least 40%, 45%, 60% or 90% amino acid sequence identity to SEQ ID NO: 2 or 4 and having competence signal peptide activity or having activity for inhibiting the competence signal activity of the polypeptide of SEQ ID NO: 2 or 4, said polypeptide isolated from S.mutans

(2) fragments of SEQ.ID.NO: 2 or 4 having an amino acid sequence ranging from 1-15 amino acids removed from the N- and/or COOH terminal of SEQ ID NO: 2 or 4.

Therefore, fragments/ variants of SEQ ID NO: 2 or 4 do not meet the guidelines on written description.

The specification fails to disclose any deletion or change in (i) a peptide sequence of SEQ.ID.NO: 2 to obtain fragments/ variants at least 40%, 45%, 60% or 90% amino acid sequence identity to SEQ ID NO: 2 or 4 and having competence signal peptide activity or having activity for inhibiting the competence signal activity of S.mutans The specification does not describe any relevant structural or functional characteristics of fragments/variants in biofilm formation. None of the above variants meet the written description provision of 35

U.S.C. 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she] invented what is claimed." (See Vas-Cath at page 1116).

Thus, the specification fails to teach (1) an isolated polypeptide having at least 40%, 45%, 60% or 90% amino acid sequence identity to SEQ ID NO: 2 or 4 and having competence signal peptide activity or having activity for inhibiting the competence signal activity of the polypeptide of SEQ ID NO: 2 or 4.

(2) fragments of SEQ.ID.NO: 2 or 4 having an amino acid sequence ranging from 1-15 amino acids removed from the N- and/or COOH terminal of SEQ ID NO: 2 or 4 sufficient to allow one skilled in the art to determine that the inventor had possession of the invention as claimed.

10. Claims 25, 27-28, 38-41, 43-44, 45, 46, 47-56, 58-68 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polypeptide comprising the amino acid sequence SEQ.ID.NO 2 or 4 having S.mutans competence signal peptide activity does not reasonably provide enablement for an isolated polypeptide having at least 40%, 45%, 60% or 90% amino acid sequence identity to SEQ ID NO: 2 or 4 and having competence signal peptide activity or having activity for inhibiting the competence signal activity of the polypeptide of SEQ ID NO: 2 or 4or fragments of SEQ.ID.NO: 2 or 4 having an amino acid sequence ranging from 1-15 amino acids removed from the N- and/or COOH terminal of SEQ ID NO: 2 or 4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly

connected, to make and use the invention commensurate in scope with these claims. The claims are discussed supra

The specification fails to provide an enabling disclosure other than peptide SEQ.ID.NO: 2 or 4 itself because it fails to provide any guidance regarding how to make and use a peptide that vary by % similarity or fragments having competence signal peptide activity or having activity for inhibiting the competence signal activity of the polypeptide of SEQ ID NO: 2 or 4. The instant claims are evaluated for enablement based on the Wands analysis. Many of the factors regarding undue experimentation have been summarized in In re Wands, 858 F.2d 731,8 USPQ2d 1400 (Fed.Circ.1988) as follows:

(1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The nature of the disclosed invention is identification of polypeptide compound that inhibit or disrupt microbial biofilm involved in infections. The specification indicates that the product, peptide may be used as the target for potential anti-microbial activity. The specification, however, provides no working examples demonstrating (i.e., guidance) enablement for any fragment/variants having competence signal peptide activity or having activity for inhibiting the competence signal activity. Any deletion or change in a peptide of SEQ.ID.NO: 2 or 4 is highly complex and unpredictable. As taught by the prior art even a single amino acid change in a protein leads to unpredictable changes in the biological activity of the protein. For example, a stop codon in S.mutans strain JH1005, near at the end of the ComC coding sequence for CSP inserted after position 130 was found having low frequency (see figure 3 in Li et al 2001). Thus, it is apparent that change in a

peptide leads to loss of activity of that peptide. Furthermore, it is unclear whether peptide fragments/variants can be used for inhibiting the competence signal activity and thus must be considered highly unpredictable, requiring a specific demonstration of efficacy on a case-by-case basis.

The specification fails to provide an enabling disclosure for using peptide fragments/variants because it fails to provide guidance how a peptide fragments/variants of SEQ.ID.NO: 2 or 4 is related to CSP activity and its use in inhibiting the competence signal activity of all S.mutans strains. The specification provides no disclosure how peptide fragments/variants may be used as a target for a potential biofilm formation caused by S.mutans because it fails to provide guidance whether fragments/variants has the ability to inactivate or bind to S.mutans. Absent such demonstration, the invention would require undue experimentation to practice as claimed.

Applicant states that the instant specification discloses the fragments/variants and applicant followed the written description guidelines as required and the skilled person would understand the limitation of the claims as written.

Please note that the examiner has not rejected the claims 23,24, 26 and 42 since these claims meet the criteria for written description and enablement issues. Further, SEQ.ID.NO: 4 is not a variant or fragment as applicant states but rather it is a synthetic peptide obtained by the sequence of the processed peptide that was deduced by determining the cleavage site to be located beside the gly-gly amino acid residues (numbers 24 and 25). A peptide was synthesized (SEQ.ID.NO: 4) corresponding to amino acid sequence of residues 26-46 inclusive. This peptide has been shown to restore defective phenotypes of the comC mutants by addition of CSP, SEQ.ID.NO: 4. Therefore, it is evident that the fragments/variants obtained by various modifications of the SEQ.iD.NO:

2 or 4 would retain the activity is left for experimentation and is not disclosed in the specification.

Claim Rejections - 35 USC 112, second paragraph

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

12. Claims 49-51 and 53-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 49-51 and 53-55 are rejected as being vague and indefinite for the recitation of "capable of ". The expression "capable of " used in the claim renders the claim indefinite because the metes and bounds of the term "capable of " is unclear.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:
A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 25, 27-28, 38-41, 43-44, 45, 46, 47-56, 58-68 are rejected under 35 U.S.C. 102(b) as being anticipated by Russel 1985 ((U.S.Patent 4,521,513).

The Claims are discussed supra.
The transitional limitation "comprises" similar to the limitations, such as, "has", "includes," "contains," or "characterized by," represents open-ended claim language and

therefore does not exclude additional, unrecited elements. See M.P.E.P 2111.03 [R-1]. See Moleculon Research Corp. v. CBS, Inc., 793 F2d 1261, 229 USPQ 805 (Fed. Cir. 1986); In re Baxter, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981); Ex parte Davis, 80 USPQ 448, 450 (Bd. App.1948) ("comprising" leaves "the claim open. for the inclusion of unspecified ingredients even in major amounts". On the other hand, the limitation "consisting" of represents closed claim language and excludes any element, step, or ingredient not specified in the claim. In re Gray, 53 F. 2d 520, II USPQ 255 (CCPA 1931); Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948).

Russel discloses an isolated antigenic protein C, present in the cell walls of S.mutans and reads on the fragments/variants of SEQ.ID.NO 2 or 4 because the prior art protein (i.e., antigen or competent signal peptide) is extracted from competent bacteria S.mutans, Inbritt strain and is used to prevent dental caries from bacteria S.mutans (see column 4, lines12- 46). The antigenic protein C reads on instantly claimed polypeptide fragments/variants of SEQ.ID.NO 2 or 4 because protein c is isolated from S.mutans cell wall antigens that inherently comprise fragments/variants of SEQ.ID.NO 2 or 4

Applicant states (10/16/03) that the antigen disclosed by Russell is naturally competent but Applicants do not agree that a polypeptide SEQ ID NO: 2 is naturally made in the Inbritt strain and cell walls of S.mutans necessarily and inevitablv includes SEQ ID NO: 2 or 4 with competence signal peptide activity.

The examiner would like to bring applicant's attention to the Paragraph 58 of the instant Specification which states ' the variants retain the same or similar CSP activity as the naturally occurring CSP'. Therefore, the prior art C antigen (with CSP activity) contains several dipeptides because any two amino acids would serve as a

fragment /variant of the instantly recited fragments/variants of SEQ.ID.NO 2 or 4 since C antigen contains several peptides as stated by applicant.

(Please note that the examiner has not rejected the claims 23,24, 26 and 42 under this statue)

Remarks

15. Claims 23,24, 26 and 42 are allowed.

Claims 25, 27-28, 38-41, 43-56, 58-68 are rejected,

16. Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The RightFax number for submission of before final amendments is (703) 872-9306. The RightFax number for submission of after final amendments is (703) 872-9307.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Padma Baskar Ph.D., whose telephone number is ((571) 272-0853. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 6.30 a.m. to 4.00 p.m. except First Friday of the biweek.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose Telephone number is (571) 272-1600.

Padma Baskar Ph.D.

2/27/04

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